Furukawa CT, DuHamel T, Weimer L, et al: Cognitive and behavioral findings in children taking theophylline versus cromolyn (Abstr). J Allergy Clin Immunol 1986 Jan; 77(pt 2):186

McLoughlin J, Nall M, Isaacs B, et al: The relationship of allergies and allergy treatment to school performance and student behavior. Ann Allergy 1983 Nov; 51:506-510

Rachelefsky G, Wo J, Adelson J, et al: Behavior abnormalities and poor school performance due to oral theophylline (T) usage (Abstr). J Allergy Clin Immunol 1986 Jan; 77(pt 2):145

Springer C, Goldenberg B, Ben Dov I, et al: Clinical, physiologic, and psychologic comparison of treatment by cromolyn or theophylline in childhood asthma. J Allergy Clin Immunol 1985 Jul; 76:64-69

The Management of Asthma During Pregnancy

ASTHMA is probably the most common potentially serious medical condition to complicate pregnancy. Retrospective studies suggest that maternal asthma increases the incidence of preterm births, infants with low birth weights and perinatal deaths. Although confirmatory data are lacking, the accepted working hypothesis is that adequate control of asthma during pregnancy is the most important factor in reducing this excess risk.

Optimal management of asthma during pregnancy may involve environmental control measures, immunotherapy, medication or a combination of these approaches. Decreased exposure to avoidable triggering factors (household pets, other allergens, smoking) is an obvious, but sometimes underused, therapeutic modality. Immunotherapy is considered safe during pregnancy in women who are already deriving benefit from it; conservative dosing is recommended to minimize the chance of an anaphylactic reaction. The benefit-risk ratio does not usually favor beginning immunotherapy during pregnancy.

Pharmacologic management of asthma during pregnancy is more problematic because no asthma medication can be considered proved safe during pregnancy according to the recent Food and Drug Administration (FDA) pregnancy classification. There are a number of asthma medications, however, that appear to involve less risk during pregnancy than the risk of the uncontrolled asthma that could result if they were not used. Reassuring data in humans are available for ephedrine, theophylline, cromolyn sodium, beclomethasone dipropionate and prednisone/prednisolone. In addition, terbutaline sulfate has been used extensively in the management of premature labor, although there are no reported data in humans during early pregnancy. Inhaled bronchodilators are recommended by some authors because of their topical route and, in the case of terbutaline, the favorable FDA pregnancy classification based on reassuring animal data. The optimal sympathomimetic drug of choice for the treatment of acute asthma during pregnancy (parenterally given epinephrine or terbutaline, or mechanically nebulized bronchodilators) is not uniformly agreed upon, but, as noted above, adequate control of the asthma is the most important challenge in that situation.

Although pharmacokinetic changes have been reported to occur during pregnancy, theophylline is the only asthma medication for which gestational pharmacokinetic data are available. One study of ten pregnant women with asthma suggests that the clearance of theophylline may be prolonged during later pregnancy but that the weight-corrected volume of distribution does not change during pregnancy. Thus, the recommendations for milligram-per-kilogram loading doses of theophylline do not need to be altered during pregnancy, but maintenance doses may need to be reduced. Because the data reveal significant interpatient variation in gestational theophylline pharmacokinetics, determining theophylline concentrations at least once each trimester is recommended in pregnant patients receiving theophylline regularly.

MICHAEL SCHATZ, MD
San Diego

REFERENCES

Greenberger PA, Patterson R: Management of asthma during pregnancy. N Engl J Med 1985; 312:897-902

Millstein LG: FDA's 'pregnancy categories' (Letter). N Engl J Med 1980 Sep 18; 303:706

Schatz M, Zeiger RS, Mellon M, et al: Asthma and allergic diseases during pregnancy: Management of the mother and prevention in the child, *In* Middleton E Jr, Reed CE, Ellis EF (Eds): Allergy: Principles and Practice, 2nd Ed. St Louis, CV Mosby, 1983, pp 935-986

Nonsedating Antihistamines in the Treatment of Allergic Disease

ALTHOUGH THE EFFECTS OF HISTAMINE have been known for 75 years, it was not until 1937 that Daniel Bovet was able to antagonize this mediator with the first antihistamine, compound 929F. Although he received a Nobel prize for his work, this compound was too toxic for human use. Now, more than 50 different antihistamines in six different classes are available by prescription or over the counter in the United States.

We now know that there are H_1 and H_2 histamine receptors, but we are most concerned with H_1 receptor activity in cases of allergy, whereas H_2 receptors primarily regulate gastric secretion of hydrochloric acid. The effects of classic antihistamines on H_1 receptors in the central nervous system, with resulting sedation and their anticholinergic effect on mouth dryness, limit their usefulness in many patients. The unwanted effects of sedation are due primarily to the lipid solubility of these older compounds, which allows them to cross the blood-brain barrier into the central nervous system and affect the H_1 receptors in the brain. The newer nonsedating antihistamines are often analogues or even active metabolites of classic antihistamines. Their molecular structure, however, interferes with passage into the brain. Many of the new nonsedating antihistamines are currently under clinical development, but three drugs—astemizole, mequitazine and terfenadine—are available for use in many countries.

In May 1985, terfenadine (Seldane) was approved for use in the United States as a 60-mg tablet to be administered twice a day for the treatment of seasonal allergic rhinitis. This compound has been shown to be an effective H_1 receptor antagonist for most patients with allergic rhinitis. In clinical trials, the incidence of sedation has been no greater than that reported by patients taking a placebo. Twice-a-day dosing increases patients' compliance, and the lack of central nervous system and anticholinergic side effects encourages continued use. Activity is seen in most patients after a single dose, but maximum response may not occur for three days.

Astemizole is currently available in many countries as a 10-mg tablet and should be given approval by the Food and Drug Administration for use in the United States by spring